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Supplemental Amendment for application 10/037, 718 Applicants MCGINNIS ET AL.
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In the Claims

Please amend and add the following claims according to the following listing of claims under 37 CFR 1.121.

Listing of Claims under 37 CFR 1.121:

1-5 (CANCELED)

6. (PREVIOUSLY AMENDED): A process for identifying one or more bi-allelic markers linked to a bi-allelic trait-causing polymorphism in a species of creatures, comprising the acts of:

- a) choosing two or more bi-allelic covering markers so that a CL-F region is systematically covered by the two or more covering markers, the CL-F region being a collection of one or more points on a two-dimensional map, the two-dimensional map having the two dimensions of chromosomal location and least common allele frequency;
- b) choosing a statistical linkage test based on allelic association for each covering marker;
- c) choosing a sample of individuals for each covering marker;
- d) obtaining genotype data/sample allele frequency data for each covering marker and the sample chosen for each covering marker, and obtaining phenotype status data for the trait for each individual in the sample chosen for each covering marker;
- e) calculating evidence for linkage between each covering marker and the trait-causing polymorphism using the statistical linkage test based on allelic association chosen for each covering marker and the genotype data/sample allele frequency data for each covering marker and using the phenotype status data for the trait for each individual in the sample chosen for each covering marker obtained in d); and
- f) identifying those covering markers as linked to the trait-causing polymorphism which show evidence for linkage based on the calculations of e).

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7. (PREVIOUSLY AMENDED): A process as in claim 6, wherein the CL-F region is for a species, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

8. (PREVIOUSLY AMENDED): A process as in claim 7, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and whereby the segment of the segment-subrange is a chromosome segment and the length of the chromosome segment is less than or equal to the length of the chromosome.

9. (PREVIOUSLY AMENDED): A process as in claim 6, wherein the CL-F region is for a species, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of covering markers are not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage, wherein a chromosome or a chromosomal subregion of interest is completely covered by chromosomal segments, wherein the segments may or may not overlap, wherein the segments are short enough that polymorphisms within each segment are likely to be in linkage disequilibrium with each other, wherein each covering marker belongs to a subset of covering markers, wherein there is more than one marker in each subset, whereby there are two or more markers in each subset, wherein the markers in each subset have approximately the same allele frequencies, wherein the difference between the least common allele frequencies of any two markers in a subset does not exceed 0.15, wherein the markers in each subset are located within one segment and within each segment there are five subsets, or more or less than five subsets of covering markers, wherein the approximate allele frequencies of the markers in each subset are spaced approximately evenly over a subrange.

10. (CANCELED)

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11. (PREVIOUSLY AMENDED): A process as in claim 7, wherein the species is not human being.

12. (CANCELED)

13. (CANCELED):

14. (PREVIOUSLY AMENDED): A process as in claim 7, wherein the process uses thousands of bi-allelic covering markers.

15. (PREVIOUSLY ADDED): A process as in claim 6, further comprising the act of:

f) localizing the trait-causing polymorphism to the chromosomal location-least common allele frequency (CL-F) location of one or more markers that show evidence for linkage based on the calculations of act e), wherein the localizing uses a technique or techniques that detects gradients, wherein the detection technique or techniques uses a gradient along the allele frequency dimension.

16. (PREVIOUSLY AMENDED): One or more copies of a set of oligonucleotides, the set of oligonucleotides being complementary to a group of two or more bi-allelic covering markers of the same species, wherein the group of covering markers systematically cover a CL-F region, the CL-F region being a collection of one or more points on a two-dimensional map, the two-dimensional map having the two dimensions of chromosomal location and least common allele frequency.

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17. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 16, wherein each oligonucleotide in the set is a type (1) complementary oligonucleotide or-wherein each oligonucleotide in the set is a type (2) complementary oligonucleotide, wherein each bi-allelic covering marker is an exact, true bi-allelic marker, wherein the CL-F region is for a species, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

18. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and whereby the segment of the segment-subrange is a chromosome segment and the length of the chromosome segment is less than or equal to the length of the chromosome.

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19. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 16, wherein each oligonucleotide in the set is a type (1) complementary oligonucleotide-~~or wherein each oligonucleotide in the set is a type (2) complementary oligonucleotide~~, wherein the CL-F region is for a species, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of covering markers are not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage, wherein a chromosome or a chromosomal subregion of interest is completely covered by chromosomal segments, wherein the segments may or may not overlap, wherein the segments are short enough that polymorphisms within each segment are likely to be in linkage disequilibrium with each other, wherein each covering marker belongs to a subset of covering markers, wherein there is more than one marker in each subset, whereby there are two or more markers in each subset, wherein the markers in each subset have approximately the same allele frequencies, wherein the difference between the least common allele frequencies of any two markers in a subset does not exceed 0.15, wherein the markers in each subset are located within one segment and within each segment there are five subsets, or more or less than five subsets of covering markers, wherein the approximate allele frequencies of the markers in each subset are spaced approximately evenly over a subrange.

20. (CANCELED):

21. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein the species is not human being.

22. (CANCELED)

23. (CANCELED):

24. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein there are thousands of bi-allelic covering markers.

25. (CANCELED)

26. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein thousands of the covering markers are from one chromosome.

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27. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein y is 0.2 and x is 12 cM.

28. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein there are thousands of covering markers and the species is not human being.

29. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 18, wherein thousands of covering markers are from the chromosome, wherein the species is a paleospecies, a species hybrid, an agamospecies, an ecosystem species or a plant species.

30. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 17, wherein the species is not human being and the density of covering markers is at least thousands per chromosome or wherein thousands of the covering markers are from one chromosome.

31. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 30, wherein the species is a paleospecies, a species hybrid, an agamospecies, an ecosystem species or a plant species.

32. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 19, wherein each bi-allelic covering marker is an exact, true bi-allelic marker, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and wherein the segment of the segment-subrange is the subregion of interest or the chromosome, whereby the CL-F region is a rectangular region defined by the chromosome or subregion of interest in the chromosomal location dimension and defined by the subrange in the allele frequency dimension, wherein each point in the CL-F region is N-covered to within [L, y] by markers belonging to a single subset, L is the length of the longest segment of the segments that cover the chromosome or subregion of interest, y is 0.15 and N ≥ 2.

33. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides as in claim 32, wherein the subrange of the segment-subrange is the subrange 0 to less than 0.1.

34. (CURRENTLY AMENDED): A-copyOne or more copies of a set of oligonucleotides in claim 32, wherein N > 2.

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35. (PREVIOUSLY AMENDED): A process as in claim 9, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and wherein the segment of the segment-subrange is the subregion of interest or the chromosome, whereby the CL-F region is a rectangular region defined by the chromosome or subregion of interest in the chromosomal location dimension and defined by the subrange in the allele frequency dimension, wherein each point in the CL-F region is N-covered to within [L, y] by markers belonging to a single subset, L is the length of the longest segment of the segments that cover the chromosome or subregion of interest, y is 0.15 and N ≥ 2.

36. (PREVIOUSLY ADDED): A process as in claim 35, wherein the subrange of the segment-subrange is the subrange 0 to less than 0.1.

37. (PREVIOUSLY AMENDED): A process as in claim 35, wherein no two covering markers in a single subset is a redundant pair of markers in extreme positive linkage disequilibrium that provide nearly identical information with respect to their linkage and association with a third polymorphism, and wherein the inclusion of a bi-allelic marker in the subset so that there would be a redundant pair in the subset would not increase the likelihood of detecting linkage and association of the trait-causing polymorphism, wherein N > 2.

38. (PREVIOUSLY AMENDED): A process as in claim 8, wherein there are thousands of covering markers from the chromosome.

39. (PREVIOUSLY ADDED): A process for obtaining genotype data/sample allele frequency data for each bi-allelic marker of a group of two or more bi-allelic covering markers in the chromosomal DNA of one or more individuals of a sample, each individual in the sample being a member of the same species, comprising:

a) determining information on the presence or absence of each allele of each bi-allelic marker of a group of two or more bi-allelic covering markers in the chromosomal DNA of one or more individuals of a sample, a CL-F region being systematically covered by the two or more bi-allelic covering markers, the CL-F region being a collection of one or more CL-F points on a two-dimensional map, the two-dimensional map having the two dimensions of chromosomal location and least common allele frequency; and

b) transforming the information of step a) into genotype data/sample allele frequency data for each marker of the group.

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45. (PREVIOUSLY AMENDED): An apparatus as in claim 44, wherein the CL-F region is for a species, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

46. (PREVIOUSLY AMENDED): An apparatus as in claim 45, wherein the apparatus is a high-density array of oligonucleotides or the apparatus is oligonucleotides bound to a glass slide or a silicon chip, wherein each covering marker is an exact, true bi-allelic marker.

47. (PREVIOUSLY AMENDED): An apparatus as in claim 46, wherein thousands of covering markers are from one chromosome.

48. (PREVIOUSLY ADDED): An apparatus as in claim 47, wherein the species is not human being.

49. (PREVIOUSLY AMENDED): An apparatus as in claim 46, wherein the species is not human being and there are thousands of covering markers from one chromosome.

50. (PREVIOUSLY AMENDED): An apparatus as in claim 46, wherein the species is not human being and the density of covering markers is at least thousands per chromosome.

51. (PREVIOUSLY AMENDED): An apparatus as in claim 49, wherein there are thousands of covering markers or the density of covering markers is at least thousands per chromosome and wherein the species is not human being and the species is a paleospecies, a species hybrid, an agamospecies, an ecosystem species or a plant species.

52. (PREVIOUSLY ADDED): An apparatus as in claim 46, wherein thousands of covering markers are from one chromosome.

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53. (PREVIOUSLY ADDED): An apparatus as in claim 46, wherein the density of covering markers is at least thousands per chromosome.

54. (PREVIOUSLY ADDED): An apparatus as in claim 46, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and whereby the segment of the segment-subrange is a chromosome segment and the length of the chromosome segment is less than or equal to the length of the chromosome, wherein thousands of covering markers are from the chromosome.

55. (CANCELED)

56. (PREVIOUSLY ADDED): A process as in claim 40, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and whereby the segment of the segment-subrange is a chromosome segment and the length of the chromosome segment is less than or equal to the length of the chromosome, wherein thousands of covering markers are from the chromosome.

57. (NEW): A process as in claim 40, wherein the process is for genotyping an individual, comprising: a) genotyping an individual of the sample at the two or more bi-allelic covering markers.

58. (NEW): A process as in claim 57, wherein each covering marker is an exact, true bi-allelic marker.

59. (NEW): A process as in claim 58, wherein there are thousands of covering markers.

60. (NEW): A process as in claim 59, wherein thousands of covering markers are from one chromosome.

61. (NEW): A process to obtain genotype data/sample allele frequency data, comprising: obtaining genotype data/sample allele frequency data for each of two or more bi-allelic covering markers, wherein the covering markers systematically cover a CL-F region.

62. (NEW): A process as in claim 61, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

63. (NEW): A process as in claim 62, wherein x is 12 cM and y is 0.2.

64. (NEW): A process as in claim 63, wherein the data is genotype data.

65. (NEW): A process as in claim 63, wherein there are thousands of covering markers.

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66. (NEW): A process as in claim 64, wherein there are thousands of covering markers.
67. (NEW): A process as in claim 64, wherein thousands of covering markers are from one chromosome.
68. (NEW): One or more copies of a set of oligonucleotides as in claim 17, wherein the CL-F region is a segment-subrange, wherein the width of the subrange of the segment-subrange is less than 0.5 and whereby the segment of the segment-subrange is a chromosome segment and the length of the chromosome segment is less than or equal to the length of the chromosome, wherein thousands of covering markers are from the chromosome.
69. (NEW): One or more copies of a set of oligonucleotides as in claim 16, wherein each oligonucleotide in the set is a type (2) oligonucleotide and wherein each oligonucleotide has utility as a PCR primer, wherein each bi-allelic covering marker is an exact, true bi-allelic marker, wherein the CL-F region is for a species, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.
70. (NEW): One or more copies of a set of oligonucleotides as in claim 69, wherein y is 0.2 and x is 12 cM, wherein there are thousands of covering markers.

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71. (NEW): Oligonucleotides with utility as PCR primers to obtain genotype data/sample allele frequency data by generating a physico-chemical signal, wherein the genotype data/sample allele frequency data is for each of two or more bi-allelic covering markers, wherein a CL-F region is systematically covered by the two or more covering markers, wherein the CL-F region is for a species, whereby the oligonucleotides include copies of a set of oligonucleotides, the set of oligonucleotides being complementary to the group of two or more bi-allelic covering markers of the species, wherein the CL-F region is N covered to within [x, y] by the two or more bi-allelic covering markers, wherein x is less than or equal to about D_{CL} or the equivalent thereof and y is less than or equal to about 0.2, D_{CL} is equal to the largest chromosomal length, computed by any method, for which linkage disequilibrium has been observed between any polymorphisms in any population of the species, wherein x is short enough that it is possible for polymorphisms within the chromosomal location distance x of each other to be in linkage disequilibrium, N is an integer greater than or equal to 1, wherein the choice of covering markers is not based on the assumption that a covering marker is the trait-causing polymorphism, wherein the group of two or more covering markers is not an essentially one-dimensional panel of markers for a linkage study, wherein the essentially one-dimensional panel is a panel not based on using similarity of marker allele frequency and possible trait-causing polymorphism allele frequency to increase the power of an association-based linkage test to detect evidence for linkage.

72. (NEW): Oligonucleotides as in claim 71, wherein each bi-allelic covering marker is an exact, true bi-allelic marker.

73. (NEW): Oligonucleotides as in claim 72, wherein the data is genotype data, and wherein y is 0.2 and x is 12 cM.

74. (NEW): Oligonucleotides as in claim 73, wherein there are thousands of covering markers.

75. (NEW): Oligonucleotides as in claim 73, wherein thousands of covering markers are from one chromosome.

76. (NEW): Oligonucleotides as in claim 73, wherein the species is not human.

77. (NEW): Oligonucleotides as in claim 75, wherein the species is not human.

78. (NEW): Oligonucleotides as in claim 76, wherein the species is a paleospecies, a species hybrid, an agamospecies, an ecosystem species or a plant species.

79. (NEW): Oligonucleotides as in claim 77, wherein the species is a paleospecies, a species hybrid, an agamospecies, an ecosystem species or a plant species.

80 (NEW): Oligonucleotides as in claim 73, wherein the density of covering markers is at least thousands per chromosome.